does not define a contribution over the prior art (i.e. Boyle US Patent No. 5,843,678). Applicants respectfully traverse.

Applicants submit that the Examiner has improperly applied the PCT unity of invention guidelines. Under unity of invention practice, the Examiner should determine whether there is unity between the most generic claim and the remaining claims rather than determining that anticipation of a single independent claim (allegedly claim 54) renders all the remaining claims non-unitary. The broadest claim in the instant application is claim 1. Contrary to the Examiner's assumption, Applicant submits that the unifying feature of claim 1 is the concept of actively immunizing against autologous OPGL so as to break autotolerance. Whether one uses protein vaccination, DNA vaccination or live vaccination is, in that context, not an important issue. It is important to note that the Examiner has not indicated that the Boyle reference anticipates this claim. Boyle does not teach breaking of autotolerance towards autologous OPGL. The fact that the Examiner has not cited the Boyle patent against claim 1 confirms this fact.

As set forth in the Annex B of the PCT Administrative Instructions:

"(e) Combination of Different Categories of Claims. <u>The method for determining unity of invention under Rule 13 shall be construed as</u>

permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:

(i) in addition to an independent claim for a given product, an independent claim for a process specifically adapted for the manufacture of the said product, and an independent claim for the use of the said product, or

(ii) **in addition to an independent claim for a given process, an independent claim for an apparatus or means specifically designed for carrying out the said process**, or

(iii) in addition to an independent claim for a given product an independent claim specifically adapted for the manufacture of the said product and an independent claim for an apparatus for an apparatus or means specifically designed for carrying out the said process . . .etc." (emphasis added).

As indicated by the guidelines, if the subject matter of generic claim 1 is not anticipated, the claims relating to "means specifically designed for carrying out the process of claim 1" are unitary therewith. This encompasses every molecule or composition that is capable of specifically breaking self-tolerance towards OPGL. Further support for the unity of invention may be found in

Example 17 of Annex B which finds unity between a novel protein and a nucleic acid fragment encoding it. Under the PCT unity of invention guidelines, it is clear that claims to both the OPGL variants, DNA encoding the OPGL variants, adjuvant formulations of OPGL variants, production methods of OPGL variants, etc. should be allowed in the same application if the features all relate to the same special technical feature of the main independent and generic claims which, in this case, is the breaking of autotolerance in an animal against autologous OPGL.

In view of the above, Applicants respectfully request reconsideration and removal of the restriction requirement. Although applicants strongly traverse, to comply with 37 CFR 1.143, Applicants elect Group I, namely claims 1-24 and 28, in part, drawn to a method for *in vivo* down regulation of osteoprotegerin ligand activity in an animal comprising administering a protein. Applicants further elect human OPGL (SEQ ID NO: 2) as the single OPGL polypeptide and the truncated human OPGL (residues 159-317) where residues 257-262 are substituted with an inserted P2 epitope (SEQ ID NO: 34) as the single OPGL structure.

Favorable consideration and early allowance of the claims is requested.

If the Examiner has any questions concerning this application, the Examiner is requested to contact the undersigned at 714-708-8555 in Costa Mesa, CA.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner of Patents and Trademarks, Washington D.C. 20231 on: 8-5-02
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August 5, 2002
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